REMARKS/ARGUMENTS

The Examiner queried the status of claim 41. Claim 41 is cancelled, as noted by the Examiner and as indicated in the listing of claims above.

The Examiner required the submission of corrected drawings having regard to the PTO-948 appended to Paper No. 7. The objection raised was with respect to the left margin of Figures 2A and 2B. New Figures 2A and 2B are enclosed to replace current Figures 2A and 2B with the correct margin size.

Claims 15 to 24, 27, 28 and 49 have been cancelled to avoid double-patenting with respect to claims pending in copending Application No. 09/272,262, as discussed below.

The Examiner objected to the claims with respect to the recitation of nucleotide sequences encoding introns. Claim 1 now has been corrected to refer to the second nucleotide sequence comprising an intron.

The withdrawal of the rejections of claims 1 to 9, 13 to 23, 27 to 34 and 39 to 42 under 35 USC 112, first paragraph, is gratefully acknowledged.

The Examiner rejected claims 1 to 9, 13 to 23, 27, 28, 30 to 34, 39 and 49 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In this regard, the Examiner objected to the term "plasmid which will not replicate". The simply the language, claim 1 now refers to a plasmid. Having regard thereto, it is submitted that an indefiniteness has been removed.

It is submitted, therefore, that the rejection of claims 1 to 9, 13 to 23, 27, 28, 30 to 34, 39 and 49, as amended and insofar as they remain in the application, under 35 USC 112, second paragraph, should be withdrawn.

The Examiner rejected claims 1 to 2, 5 to 7, 15 to 16, 19 to 20, 30 to 34 and 49 under 35 USC 103(a) as being unpatentable over Olmsted et al and Simard et al in view of Johnson et al, Wagener et al, Norman et al and Haddad et al. Of these claims, claims 15 and 16, 19 and 20, 30 to 34 and 49 have been deleted.

Claim 1 has been amended to recite that the composition produces a balanced Th1/Th2 cytokine profile.

The Olmsted et al reference describes the provision of recombinant vaccinia viruses which encode full length or truncated versions of the human RSV G protein. These recombinants were utilized in the intranasal immunization of rats. Olmsted also describes the sequencing of the RSV G protein from three strains of RSV. The constructs provided and utilized in Olmsted et al are vaccinia virus recombinants. These are not plasmid vectors and nor is there specified a promoter in a plasmid vector operable to direct expression of RSV G protein *in vivo*.

Simard et al also describes recombinant vaccinia viruses, this time containing a specific fragment encoding amino acid 124 to 203 of the RSV G protein. Again a plasmid vector and the promoter described by applicant are not described. In addition, the RSV G fragment described in Simard does not correspond to any of the sequences identified by SEQ ID in claim 1. As the Examiner notes, Simard et al point out on page 313, the vaccinia virus is not expected to become a suitable vector for the development of human vaccine in the future.

In support of the patentability of the claims of this application, there was previously submitted a scientific paper of Li et al which corresponds to the data presented in the application. With respect to the paper, the plasmid pXL5 referred to in the specification has been renamed p34M7A and the plasmid pXL6 has been renamed p41M2 in the paper.

Applicants claims are all directed to the use of a plasmid vector which contains the nucleotide sequence encoding RSV G protein or a RSV G protein fragment that generates antibodies that specifically react with RSV G protein. As set

forth in the specification, for example, on page 8, lines 9 to 10 and page 30, lines 26 to 35, the administration of the plasmid to a host produces a balanced Th1/Th2 cytokine profile.

The scientific paper by Li et al describes the problems in the art of an unbalanced cytokine response (page 54, right hand column) as well as problems with using vaccinia (page 55, 2nd paragraph, left hand column). From this prior work, a person skilled in the art would draw the conclusion that the RSV G proteins had an inherent bias towards Th2 cytokine production and there would be no expectation that a different result would be obtained using a DNA plasmid vector from that obtained using a vaccinia virus vector. At the time of this invention it was not known that in vivo expression of the G protein of RSV in a DNA vector would result a shifting of the immune response to a more balanced one regardless of the route of administration, in contrast to the vaccinia work (see page 59, first paragraph of Discussion). This result, it is submitted, is an unexpected result.

It is clear, therefore, that there is a prejudice in the art against using RSV G glycoprotein in any form, in that a Th2 cytokine response has to be expected, a response associated with the highly undesirable immunopotentiation. In the face of this prejudice in the art, applicants took a plasmid DNA vector approach to DNA immunization of RSV G protein and to their surprise, found that, not only did this approach result in protection in the mouse model, but no immunopotentiation was observed in cotton rats and a balanced Th1/Th2 cytokine profile was obtained.

In the Office Action, the Examiner noted this discussion of the obtaining of a balanced Th1/Th2 cytokine profile and commented:

> "..... it is noted that the features upon which applicant relies (i.e. the administration of the plasmid to the host produces a balanced Th1/Th2 cytokine profile) are not recited in the claims."

Claim 1 now has been amended to recite this feature, as discussed above.

It is submitted that there is nothing in the secondary references which have been cited which even suggests that this result may be obtained by replacing the vaccinia virus vector with a plasmid vector, as in the present invention.

Johnson et al is said to supplement both Olmsted and Simard by providing the amino acid sequence of the G protein derived from the Long strain of RSV which is 99.1% identical to SEQ ID No: 2. As the Examiner notes, Olmsted and Simard differ from the instant invention in that they use vaccinia virus.

The Wagener et al reference is concerned with induction of antibodies against SIV and, therefore, is wholly irrelevant to RSV. Norman et al apparently is cited for disclosing a plasmid vector for gene expression including a CMV promoter and enhancer and the CMV IE intron A. Haddad et al is cited for the limitation of the tPA signal sequences.

None of these references contain any teaching which would overcome the inherent prejudice in the art against using RSV G glycoprotein in any form, as set forth above.

Accordingly, it is submitted that claims 1 to 2, 5 to 8, 15 to 16, 19 to 20, 30 to 34 and 49, in their amended form and insofar as the remain in the application, are patentable over the applied art and hence the rejection of these claims under 35 USC 103(a) as unpatentable over the cited combination of prior art should be withdrawn.

The Examiner rejected claims 1 to 2, 5 to 7, 15 to 16, 19 to 20, 30 to 34 and 49 under 35 USC 103(a) as being unpatentable over Stott et al and Johnson et al taken with Simard et al, Wagener et al and Haddard et al in further view of Herrmann et al.

This rejection is basically a restatement of the previous rejection with Stott et al replacing Olmsted et al and with the addition of Herrmann et al.

The Stott et al reference describes a vaccinia vector which expresses RSV G protein in rabbits. It remains the case that, while Simard et al suggests that

vaccinia virus may not be the vector of choice for humans, there was an inherent prejudice in the art that the various vaccine approaches based on RSV G protein produced enhanced pulmonary disease attributed to an imbalanced cell-mediated immune response of the Th2 type, as described in the Li et al article. Having regard thereto, there would be no expectation by a person skilled in the art that a plasmid vector would produce any other result. Accordingly, it is submitted that applicants results are surprising.

It is submitted that the Herrmann reference adds nothing to the other references. As the Examiner indicates, the reference discloses a plasmid vector having a promoter operatively linked to a nucleotide sequence encoding a rotavirus polypeptide being expressed in a cell of a mammal administration with the plasmid vector. This disclosure is limited to rotavirus and provides no suggestion to provide a plasmid vector containing a promoter and nucleotide sequences encoding RSV G protein.

Accordingly, it is submitted that claims 1, 2, 5 to 7, 15 to 16, 19 to 20, 30 to 34 and 49, as amended and insofar as they remain in the application, are patentable over the applied combination of prior art and hence the rejection thereof under 35 USC 103(a) as being unpatentable over the newly applied combination of prior art, should be withdrawn.

The Examiner provisionally rejected claims 15, 16, 17, 18, 19, 20, 21, 22, 23, 30 to 34 and 39 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 15 to 28 and 30 to 39 of copending Application No. 09/272,262.

Although the rejection is a provisional one because the conflicting claims have not in fact be patented, these claims have been deleted from this application, thereby rendering the rejection moot.

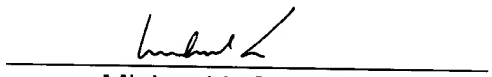
The Examiner provisionally rejected claims 1 to 9, 13 to 23, 27 and 28 under the judicially-created doctrine of obviousness-type double patenting as being

unpatentable over claims 1, 6, 7, 10, 11, 13 and 14 of copending Application No. 08/896,442.

The rejection is a provisional one because the conflicting claims have not in fact been patent. Having regard thereto, it is submitted that the resolution of this matter may be deferred.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,



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